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ELECTRODES FOR FUNCTIONAL NEUROMUSCULAR STIMULATION

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B.3 Electrode Materials

Abstract

In vivo testing of alternative silicone rubber and fluoropolymer materials used in the manufacture of electrodes has been performed and described previously. In this quarter, additional studies involving another silicone rubber formulation that may have improved surface properties were begun. Silicone rubber nerve cuffs made from this material were implanted on the sciatic nerves of 6 rats. After 2 and 4 weeks, the animals were killed by aortic perfusion and the tissue surrounding the implants was kept for histological processing.

Background

The basis for these studies has been described in detail in the previous two progress reports (QPRs #8 and #9). Briefly, the original materials used in the construction of our nerve cuff electrodes are no longer available for long-term implant applications. The alternative materials that we have identified are being investigated in these studies to determine their equivalence in terms of cellular encapsulation and neural tissue response.

The silicone rubber sheeting that is being replaced was made from Dow Corning's Silastic Q7-4550, a material that is no longer available for long-term implant. Working with Specialty Silicone Fabricators and NuSil Silicone Technology, we have ordered and purchased 50-75 μm thick sheeting made from three different silicone rubber formulations in an effort to replace the Dow product.

The first order of sheeting was made from a liquid silicone rubber, NuSil's MED-4840, to a final thickness of 75 μm. However, because of the physical and handling properties of the uncured material, the fabricators had difficultly in processing the material into sheeting and felt that 75 μm thickness was the limit of their fabrication capabilites for that specific silicone rubber formulation. They recommended that we investigate a silicone rubber liquid dispersion that would likely be easier to process. Using what is known as a knife-coating technique, they expected that the sheeting could be made to a 50 μm thickness, which is a more appropriate thickness for our cuff electrodes.

Therefore, our second batch of 'replacement' sheeting was 50 μm in thickness and was made from the NuSil liquid dispersion product MED2-6400. This sheeting was used in the manufacture of cuff electrodes and preliminary observations were made. Mechanically, the sheeting seemed appropriate for cuff manufacture and perhaps even improved over the Dow Corning sheeting. However, the material was very tacky or 'sticky' when handled. This additional tackiness made the cuff manufacturing process more cumbersome as well as making handling and manipulation of completed cuffs more difficult. We felt that we could accept the increased

difficulties in the manufacturing process, but had significant concerns regarding how the additional tackiness might reduce ease of implant and in vivo performance. Any handling problems with the cuff could be expected to create excess stress on the nerve during implant. Additionally, the stickiness might interfere with the self-sizing properties of the cuff, preventing cuff compliance with nerve swelling or shrinking.

These concerns were discussed with our material supplier, NuSil. They suggested we investigate the use of a special formulation of theirs that had been developed specifically for reduced surface tackiness. This special formulation contains an additional surface flattening agent (a silica) that lays on the surface layer of the final product and reduces the tackiness. They stressed, however, that the biocompatibility of this product was unknown.

It was decided to investigate this material, and our third batch of replacement sheeting was 50μm in thickness and made from the NuSil liquid dispersion product, MED2-6641-1. This sheeting has been received and it is striking in that the addition of the flattening agent made the sheeting white in color, rather than the transparent, almost colorless appearance of the other two sheeting batches. Preliminary observations made while handling the material and using it in cuff manufacture are that it does have reduced surface tackiness. Additionally, the mechanical properties do not appear to be grossly different than those of the second sheeting batch, the MED2-6400 sheeting.

Cuffs made from both the Dow Corning material and the replacement NuSil MED2-6400 sheeting were used in the animal studies reported in QPR #9. The additional animal studies that were undertaken and are reported here involved cuffs made from the third replacement sheeting, NuSil's MED2-6641-1, which had not been received at the time of the original animal study.

Methods

The study design and methods largely followed that reported in QPR #9. Silicone rubber nerve cuff electrodes, all fabricated from NuSil MED2-6641-1 were implanted on the sciatic nerves of adult rats. Cuffs with leads were placed on the animal's left side, and cuffs without leads were placed on the right side. In 2 animals, segments of wire were inserted subcutaneously along the animal's back. These implants were intended to replace those that were found missing upon explant in the previous animal study. Two and 4 weeks after implantation, the animals were killed and the tissue was fixed. Histological processing of the encapsulation tissue and implanted nerves will follow.

Implants

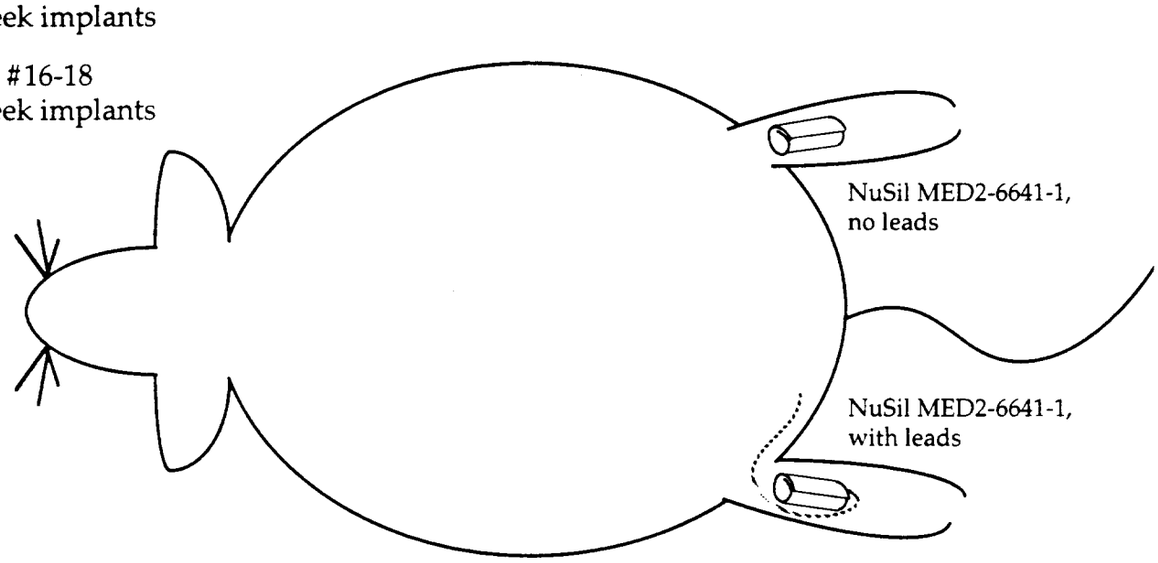
All cuffs were manufactured, cleaned, and packaged according to our standard methods and as described in QPR #9. The cuffs were manufactured to have a final inner diameter of 1 mm and were cut to a nominal length of 1 cm. All cuffs contained a backbone of three coiled wires and in half of the

cuffs this lead extended for a length of several centimeters (>10 cm) beyond the cuff.

Animal Protocol

Six adult Sprague-Dawley rats were used in the study with masses ranging from 405-550 g; 3 rats were to be implanted for 2 weeks, and 3 rats were to be implanted for 4 weeks. A schematic diagram of the implant and animal groups is provided in the accompanying figure.

Figure 1



Implant and recovery procedures were as described previously (QPR #9). Periodic observations were made of the animals throughout their implant duration. One animal (Rat #14) chewed on the skin of both hindlimbs in the area of the incision sites 3 weeks after the initial implant. The animal was re-anesthetized, the sites were cleaned and a stainless steel suture was placed on one leg. An Elizabethan collar was also placed on the rat to prevent further skin chewing. The next day, the animal was found dead; the collar may have been too tight or the animal may have been sick. The implants and nerves from this animal were harvested and placed in fixative. They will be processed for histologic staining, although we expect to see tissue necrosis due to the death of the animal that will likely mask any evaluation of the inflammatory response to the implants.

At the end of the implant period, the remaining animals were killed by aortic perfusion, following those methods described previously (QPR #9). The carcasses were placed in cold storage in glutaraldehyde and cacodylate solutions.

Future Work

The implants and surrounding tissue will be excised from the animal carcasses and specimens will be prepared for histological processing. Sectioning and histological processing of tissue from the previous study is continuing. Nerve fiber morphology at proximal, distal, and cuff-levels will be investigated. Tissue encapsulation surrounding all wire implants and the cuff electrodes will be studied for extent of inflammatory response. The inflammatory response and nerve fiber morphology from the original and both replacement materials will be compared.

Section B: Electrode Design and Fabrication
Section C: Assessment of Electrode Performance
Section D: Modifications to Improve Functional Performance

Comparison of Monopolar and Tripolar Recruitment Characteristics

In vivo studies were begun to investigate the differences in output torque vectors produced by monopolar and tripolar nerve cuff electrode stimulation. Previous work in both acute and chronic animal studies has shown that multiple contact tripolar nerve cuff electrodes can produce controlled, selective recruitment of major muscles innervated by a nerve trunk. Despite their proven performance capabilities, these multi-contact nerve cuffs present a significant challenge to clinical implementation due to the large number of associated lead wires. The twelve contact cuff electrode, used in those studies and containing 4 longitudinally arranged tripoles, requires 12 lead wires. Even with the small, very fine wires used in these electrodes, 12 leads presents difficulties in the manufacture of the electrode and connector and in the implant procedure. An electrode requiring fewer wires would ease both manufacture and implant.

In order to reduce the number of lead wires and improve the clinical feasibility of the nerve cuff electrode, we have begun investigating a simplified cuff configuration that requires only four lead wires. This simplified cuff contains monopoles, rather than tripoles. Monopolar cuff electrodes produce virtual anodes at the cuff edges. With a cuff of the same length as a longitudinally spaced tripole, the monopole cuff and its respective virtual anodes have a current flow similar to that produced by the tripolar configuration. Observations from two experiments indicate that the recruitment characteristics are very similar for the 4 contact monopolar and the 12 contact tripolar configurations.

METHODS

The study was designed so that in each animal preparation, the monopolar and tripolar electrode configurations could be compared using the *same* 12 contact cuff. This eliminates any variation in recruitment due to cuff re-positioning or surgical trauma that would likely occur if two separate cuffs had to be placed on the nerve. To compare the configurations and place the monopolar "virtual" anodes at the same sites as the tripolar "real" anodes, the length of the monopolar cuff should equal the length of the tripolar contact spacing. However, in these experiments, it was not possible to place the anodes of the tripolar configuration at the absolute edges of the cuff. Therefore, in using the same cuff for both the monopolar and tripolar stimulation, the cuff was cut as close to the outside contacts as possible in order to minimize this difference in length.

The electrodes and current flow patterns are illustrated in Figure 1. Tripolar stimulation was implemented by activating the central contact cathodically and the outside two contacts anodically. Monopolar stimulation was implemented by applying a cathodic stimulus to the central contact using a distant reference (e.g. a percutaneous needle in the nape of the neck) as the return electrode. Each contact (monopole) or longitudinal set of 3 contacts (tripole) was then referenced by its position around the nerve. Using the inside edge of the cuff as a reference, the first monopole or tripole was defined as the 0° position. The other three monopoles or tripoles were then consecutively named 90°, 180° and 270° positions, corresponding to the angle at which they lied in a cross-sectional view of the cuff around the nerve branch, as shown in Figure 2.

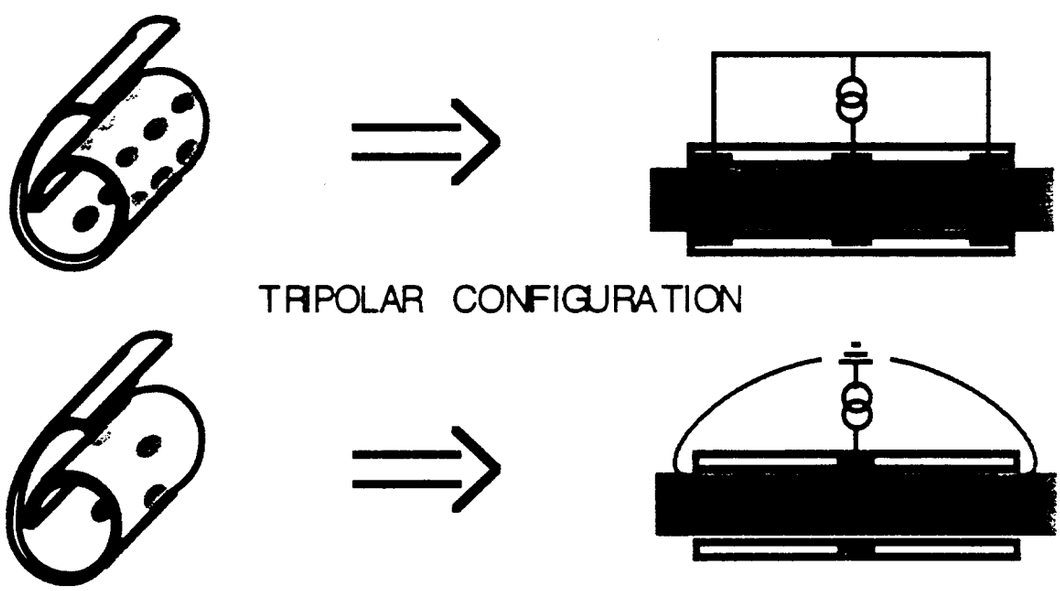


Figure 1: Comparison between a twelve contact tripolar nerve cuff (top) and a four contact monopolar nerve cuff (bottom) and their corresponding current flow. The left side shows an oblique view of the two cuffs, while the right side shows a longitudinally sectioned view of the cuffs. A symbolic representation of the current flow is also shown on the right figures. In the monopolar case, the ground symbol represents a distant return contact.

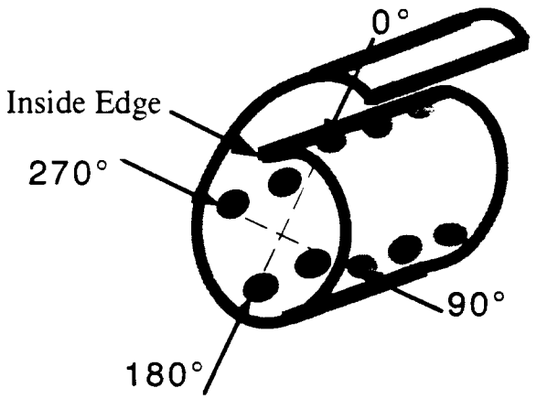


Figure 2: Definition of contact positions around the nerve cuff electrode. The 0° position is defined as the first position from the inside edge of the cuff. The remaining positions, (90°, 180°, and 270°) follow consecutively around the cuff at evenly distributed 90° intervals.

Following cuff electrode placement on the sciatic nerve of an adult cat, the incision site was closed and the animal was placed in a stereotaxic frame. Monophasic 10 μsec pulses were delivered over a range of amplitudes and the torque output about the ankle joint was measured in three dimensions by a 3 axis force transducer. The three axes about the ankle were Plantar/Dorsiflexion, External/Internal Rotation, and Eversion/Inversion. Total torque output can be graphically presented in torque space, which is a plot of the Plantar/Dorsiflexion torque versus External/Internal Rotational torque. Any one point in this torque space is representative of a vector direction and magnitude that the ankle joint is attempting to move towards. Since individual muscles tend produce a single direction of output during isometric contraction, the torque output trace graphed in torque space has a directionality consistent with the direction of that muscle's output and a length consistent with the magnitude of that muscle's force. Any change of direction in the torque output trace is taken as an indication that the activation current has spilled-over to nerve fibers that innervate a different muscle or muscle groups. The torque vectors and magnitudes generated during both monopolar and tripolar stimulation can then be used to compare the torque recruitment relationships for the two configurations.

RESULTS

Recruitment data recorded from 2 animal experiments are reported here. In Figure 3, we present both plantar flexion and lateral rotation torque with respect to the stimulus current from the first experiment. The tripolar recruitment curve (squares) is shifted to the right of the monopolar recruitment (circles) in both torque dimensions indicating that monopolar activation has a lower threshold for activation. At the largest injected current that was tested, the tripolar stimulation did not generate the same maximum torque output as that achieved with monopolar stimulation. At the time this experiment was conducted, our hardware configuration was designed to

produce a maximum current level that proved to be insufficient to achieve complete recruitment with tripolar stimulation. The hardware configuration was corrected before the next experiment was carried out.

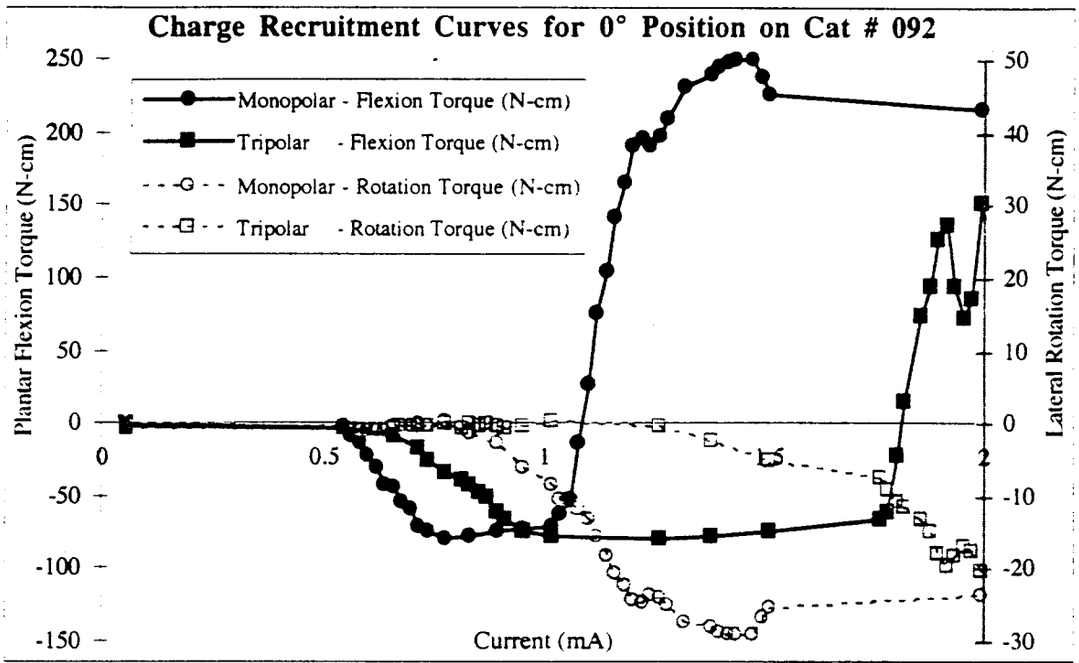


Figure 3: Graph of both plantar flexion (left vertical axis) and lateral rotation torque (right vertical axis) vs. charge. The tripolar recruitment curves (squares) are shifted to the right from the monopolar recruitment curves, due to the recruitment gain observed with monopolar stimulation. In both cases, a plateau was reached before spill-over to antagonists began.

The recruitment curve shown in Figure 3 exhibits how both monopolar and tripolar configurations reach and plateau at about full dorsiflexion (determined by supramaximal stimulation of the Common Peroneal to be about 75 N-cm of dorsiflexion). A less obvious aspect of the recruitment shown is Figure 3 is that spill-over occurs during that plateau region. After about 1/3 of the dorsiflexion plateau it was found in both configurations that medial rotation torque (a negative lateral rotation torque) started to be produced. This addition of medial rotation indicates that a new muscle is being activated. This spill-over can be better observed in torque space as shown in the upper left panel of Figure 4. The same spill-over that was difficult to see in Figure 3 is shown in Figure 4 by the sharp change in direction from the initial line progressing down to a line progressing to the

left. Information about stimulus current is omitted in a torque space presentation making it easier to compare recruitment characteristics for the two electrode configurations.

For comparison purposes, the maximum torque outputs of the four branches of the sciatic nerve (Tibial, Lateral Gastrocnemius/Soleus, Medial Gastrocnemius, and Common Peroneal) are also shown in the figure by the open circles. Stimulation at each position around the cuff was found to produce different torque outputs traces (i.e. the 0° position initially produces pure dorsiflexion and the 90° position initially produces pure medial rotation). Each of these positions produce initial torques that correspond to a different nerve branch indicating selective recruitment of the nerve fibers supplying those nerve branches.

At each of the four positions around the nerve, the monopolar and tripolar configurations generate very similar initial torque vector directions, reach spill-over at comparable torque magnitudes, and continue to produce nearly identical torque output traces after the onset of spill-over. In some cases, particularly at the 90° and 270° positions, the tripolar stimulation did not produce the full range of torque achieved with the monopolar stimulation. This outcome is attributed to the limitation of the hardware configuration, as mentioned previously.

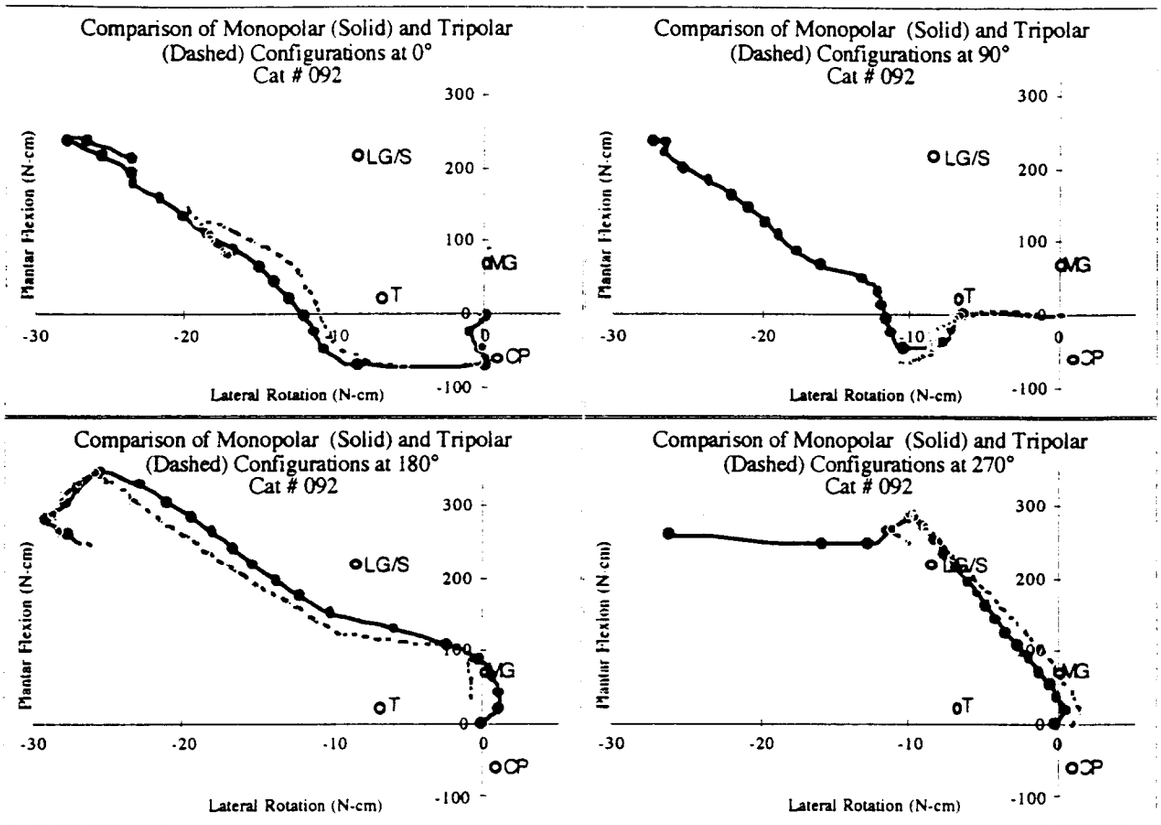


Figure 4: Comparison of output torque for monopolar and tripolar configurations at each position around the nerve trunk. The monopolar recruitment is shown by solid lines while the tripolar data is shown with dashed lines. Plantar flexion is in the positive y direction and lateral rotation is in the positive x direction. Maximum torque for branch stimulation is shown as open circles, with T indicating tibial branch, MG indicating medial gastrocnemius branch, LG/S indicating lateral gastrocnemius/soleus branch, and CP indicating common peroneal branch.

Prior to the second animal experiment, the hardware limitation was corrected. The tripolar curves from that experiment were found to extend throughout the full range of the monopolar curves, as presented in Figure 5. As in Figure 4, both the monopolar and the tripolar curves closely follow one another throughout the recruitment range. In general, the data presented in Figures 4 and 5 demonstrate that the monopolar and tripolar configurations can generate essentially equivalent torque outputs.

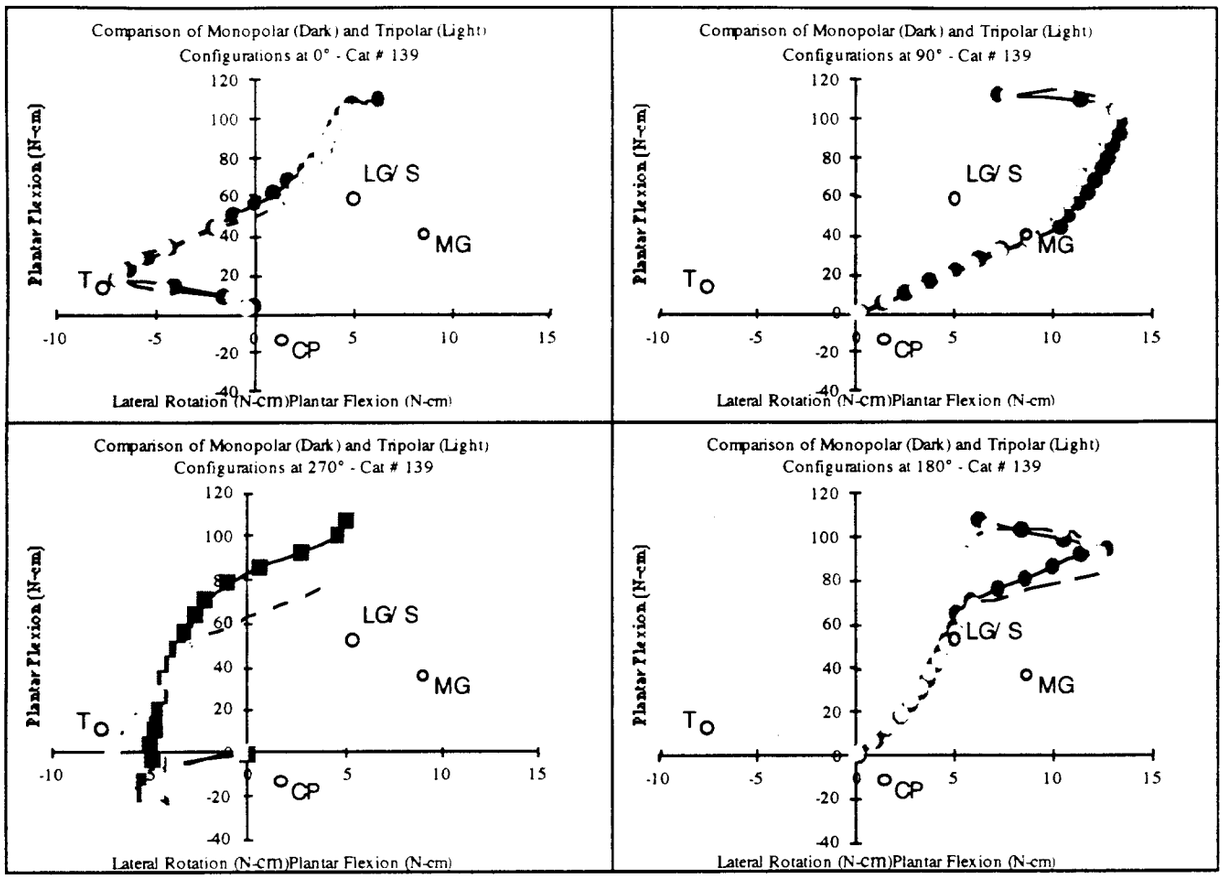


Figure 5: Comparison of monopolar and tripolar recruitment characteristics for each position around the nerve trunk in Cat #139. The monopolar recruitment is shown by dark points while the tripolar data is shown with light points. Maximum torque for branch stimulation is shown as open circles, with T indicating tibial branch, MG indicating medial gastrocnemius branch, LG/S indicating lateral gastrocnemius/soleus branch, and CP indicating common peroneal branch.

These data also indicate that after spill-over occurs, there is sometimes an increased difference in torque output between the two configurations, as can be readily seen in the lower left panel (270° position) of Figure 5. Spill-over occurs at essentially the same point in the torque space, at which point the monopolar and tripolar data begin to deviate slightly. However, the general direction of both torque output traces continue to follow similar paths. This small variation in recruitment after spill-over is also not expected to be a limitation, since most applications are targeted at stimulating individual muscles and avoiding any spill-over.

SUMMARY AND FUTURE EFFORTS

The data from these two animal experiments indicate that monopolar cuff electrode stimulation can generate a comparable recruitment range as that generated with the tripolar configuration. During the next quarter, we will work on methods to quantify the differences and complete these series of experiments.